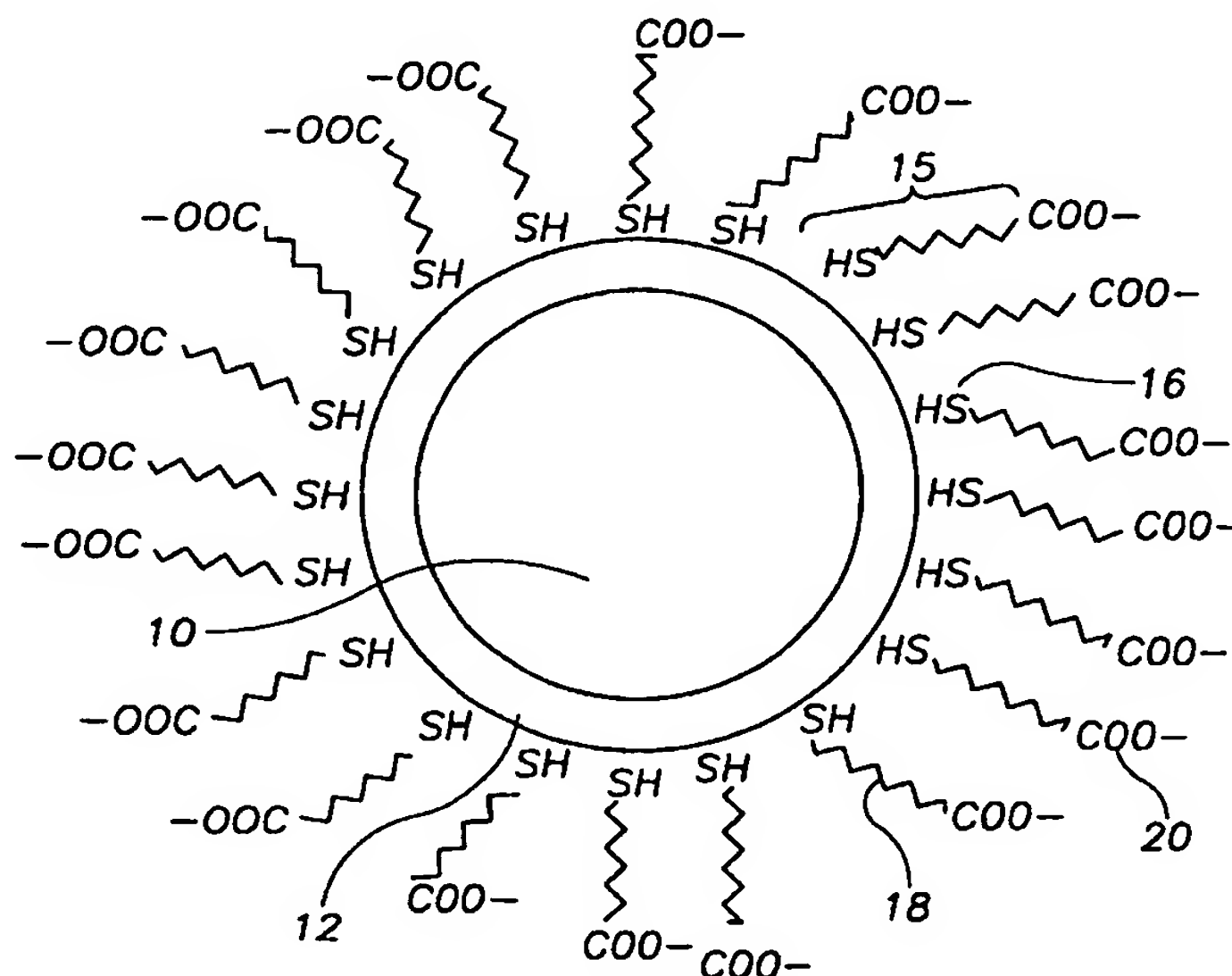




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : G01N 33/58, H05B 33/10	A1	(11) International Publication Number: WO 00/17656 (43) International Publication Date: 30 March 2000 (30.03.00)
<p>(21) International Application Number: PCT/US99/21493</p> <p>(22) International Filing Date: 17 September 1999 (17.09.99)</p> <p>(30) Priority Data: 09/156,457 18 September 1998 (18.09.98) US</p> <p>(71) Applicant: MASSACHUSETTS INSTITUTE OF TECHNOLOGY [US/US]; 77 Massachusetts Avenue, Cambridge, MA 02142 (US).</p> <p>(72) Inventors: BAWENDI, Mounji, G.; Apartment 2B, 285 Beacon Street, Boston, MA 02116 (US). MIKULEC, Frederick, V.; Apartment 2, 96 Willow Avenue, Somerville, MA 02144 (US). LEE, Jin-Kyu; 244-4, Bongchung-7-dong, Facility-Na-Dong-302, Kwanak-Gu, Seoul 151-057 (KR).</p> <p>(74) Agent: NUGENT, Elizabeth, E.; Choate, Hall & Stewart, Exchange Place, 53 State Street, Boston, MA 02109 (US).</p>		<p>(81) Designated States: JP, KR, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>

(54) Title: WATER-SOLUBLE THIOL-CAPPED NANOCRYSTALS



(57) Abstract

A water soluble semiconductor nanocrystal capable of light emission is provided, including a quantum dot having a selected band gap energy, a layer overcoating the quantum dot, the overcoating layer comprised of a material having a band gap energy greater than that of the quantum dot, and an organic outer layer, the organic layer comprising a compound having the formula: $\text{SH}(\text{CH}_2)_n\text{X}$, where X is carboxylate or sulfonate. The particle size of the nanocrystal core is in the range of about 12 Å to about 150 Å, with a deviation of less than 10 % in the core. The coated nanocrystal exhibits photoluminescence having quantum yields of greater than 10 % in water.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon	KR	Republic of Korea	PL	Poland		
CN	China	KZ	Kazakstan	PT	Portugal		
CU	Cuba	LC	Saint Lucia	RO	Romania		
CZ	Czech Republic	LI	Liechtenstein	RU	Russian Federation		
DE	Germany	LK	Sri Lanka	SD	Sudan		
DK	Denmark	LR	Liberia	SE	Sweden		
EE	Estonia			SG	Singapore		

WATER-SOLUBLE THIOL-CAPPED NANOCRYSTALS

The government has rights in this invention pursuant to National Science Foundation Grant No. DMR-9400334.

5

This application is related to the following applications which were followed in even day herewith and which are incorporated in their entirety by reference: application entitled "Inventory Control" and application entitled "Detection of Compounds and Interactions in Biological Systems Using Quantum Dots".

10

Field of the Invention

This invention relates to water-soluble nanocrystalline materials that emit visible light over narrow range of wavelengths.

15

Background of the Invention

Semiconductor nanocrystals (quantum dots) whose radii are smaller than the bulk exciton Bohr radius constitute a class of materials intermediate between molecular and bulk forms of matter. Quantum confinement of both the electron and hole in all three dimensions leads to an increase in the effective band gap of the material with decreasing crystallite size. Consequently, both the optical absorption and emission of quantum dots shift to the blue (higher energies) as the size of the dots gets smaller.

20

Bawendi and co-workers have described a method of preparing monodisperse semiconductor nanocrystals by pyrolysis of organometallic reagents injected into a hot coordinating solvent (*J. Am. Chem. Soc.*, 115:8706 (1993)). This permits temporally discrete nucleation and results in the controlled growth of macroscopic quantities of nanocrystals. Size selective precipitation of the crystallites from the growth solution can provides crystallites with even narrower size distributions. The narrow size distribution of the quantum dots allows the possibility of light emission in narrow spectral widths.

25

30

In an effort to improve the photoluminescent yield of the quantum dots, the nanocrystal surface has been passivated by reaction of the surface atoms of the quantum dots with organic passivating ligands, so as to eliminate energy levels at the

surface of the crystallite which lie within the energetically forbidden gap of the bulk interior. These surface energy states act as traps for electrons and holes which degrade the luminescence properties of the material. Such passivation produces an atomically abrupt increase in the chemical potential at the interface of the semiconductor and passivating layer (See, A.P. Alivisatos, *J. Phys. Chem.* **100**:13226 (1996)). Bawendi et al. (*J. Am. Chem. Soc.* **115**:8706 (1993)) describe CdSe nanocrystals capped with organic moieties such as tri-*n*-octyl phosphine (TOP) and tri-*n*-octyl phosphine oxide (TOPO) with quantum yields as high as 20% in organic solvents such as toluene. See also, thesis of Christopher Murray, "Synthesis and Characterization of II-VI Quantum Dots and Their Assembly into 3-D Quantum Dot Superlattices", Massachusetts Institute of Technology, September, 1995; and Kuno *et al.* (*J. Phys. Chem.* **106**(23):9869 (June, 1997)).

Although semiconductor nanocrystals prepared as described by Bawendi and co-workers exhibit near monodispersity, and hence, high color selectivity, the luminescence properties of the material is process dependent. The stability of the photoluminescent property of the nanocrystal is a function of the nature of the passivating species coating the outer surface of the nanocrystal. Known organically coated nanocrystals are not robust and exhibit degradation of photoluminescent yield in solution. This is likely due to dissociation of the passivating layer from the surface of the quantum dot or degradation of the passivating layer resulting in degradation of the semiconductor surface.

Passivation of quantum dots using inorganic materials also has been reported. Particles passivated with an inorganic coating are more robust than organically passivated dots and have greater tolerance to processing conditions necessary for their incorporation into devices. Previously reported inorganically passivated quantum dot structures include CdS-capped CdSe and CdSe-capped CdS (Than et al., *J. Phys. Chem.* **100**:8927 (1996)); ZnS grown on CdS (Youn et al., *J. Phys. Chem.* **92**:6320 (1988)); ZnS on CdSe and the inverse structure (Kortan et al., *J. Am. Chem. Soc.* **112**:1327 (1990)); ZnS-capped CdSe nanocrystals (M.A. Hines and P. Guyot-Sionnest, *J. Phys. Chem.* **100**:468 (1996); ZnSe-capped CdSe nanocrystals (Danek *et al.*, *Chem. Materials* **8**:173 (1996) and SiO₂ on Si (Wilson et al., *Science* **262**:1242 (1993)).

Kortan *et al.* describes a ZnS capped-CdSe quantum dot which has a layer of thiolphenyl groups bound to the outer surface. The thiolphenyl groups were used to passivate the surface and to allow the clusters to be isolated in powder form. Lawless *et al.* reported the preparation of CdS semiconductor nanocrystals capped with bifunctional mercaptocarboxylic acids $\text{HS}(\text{CH}_2)_n\text{COOH}$, where $n = 1-3$. TiO_2 particles were attached to the CdS dots through the functional carboxylic acid group of the bifunctional capping moiety in order to promote interparticle electron transfer between dissimilar semiconductor particles.

The quantum dots described above are soluble or dispersible only in organic solvents, such as hexane or pyridine. Many applications which rely on the fluorescent emission of the quantum dots require that the quantum dots be water-soluble.

Many reported water-soluble quantum dots suffer from significant disadvantages which limit their wide applicability. For example, Spanhel *et al.* discloses a $\text{Cd}(\text{OH})_2$ -capped CdS sol (*J. Am. Chem. Soc.* **109**:5649 (1987)); however, the photoluminescent properties of the sol was pH dependent. The sol could be prepared only in a very narrow pH range (pH 8-10) and exhibited a narrow fluorescence band only at a pH of greater than 10. Such pH dependency greatly limits the usefulness of the material; in particular, it is not appropriate for use in biological systems.

Other groups have replaced the organic passivating layer of the quantum dot with water-soluble moieties; however, the resultant derivatized quantum dots are not highly luminescent. Short chain thiols such as 2-mercaptoethanol and 1-thio-glycerol have been used as stabilizers in the preparation of water-soluble CdTe nanocrystals. See, Rogach *et al.*, *Ber. Bunsenges. Phys. Chem.* **100**:1772 (November, 1996) and Rajh *et al.*, *J. Phys. Chem.* **97**:11999 (November 1993). Other more exotic capping compounds have been reported with similar results. See, Coffey *et al.* (*Nanotechnology* **3**:69 (April, 1992) which describes the use of deoxyribonucleic acid (DNA) as a capping compound. In all of these systems, the coated quantum dots were not stable and photoluminescent properties degraded with time.

The unavailability of aqueous suspensions or solutions of quantum dots with sharp photoluminescent emissions limits their application in a variety of water-based applications, such as biological applications. In addition, aqueous solutions can often

be very aggressive chemical systems and many of the known water-soluble quantum dots systems degrade, mainly by photoanodic decomposition at the semiconductor surface interface, during long exposure times in water. Thus there remains a need for water-soluble semiconductor nanocrystals which may be prepared as stable, robust
5 suspensions or solutions in aqueous media. There is also a need for water-soluble quantum dots capable of energy emission with high quantum efficiencies, which possess a narrow particle size (and hence with narrow photoluminescence spectral range).

It is the object of the invention to provide water-soluble semiconductor
10 nanocrystals (quantum dots) which overcome the limitations of the prior art and which exhibit high quantum yields with photoluminescence emissions of high spectral purity.

Summary of the Invention

15 In one aspect of the invention, a water-soluble semiconductor nanocrystal capable of energy emission in the visible range is provided. The nanocrystal includes a quantum dot having a selected band gap energy overcoated with a layer of a material having a band gap energy greater than that of the quantum dot and with an appropriate band offset. An outer layer is found at the outer surface of the
20 overcoating layer. The outer layer includes a compound having the formula, $\text{SH}(\text{CH}_2)_n\text{X}$, where X is carboxylate or sulfonate. The affinity of the sulfur group for the nanocrystal surface promotes coordination of the compound to the quantum dot outer surface and the carboxylic moiety, with an affinity for the aqueous medium, stabilizes the aqueous suspension. In preferred embodiments, the compound may
25 have the formula, $\text{HS}(\text{CH}_2)_n\text{CO}_2\text{H}$ and salts thereof, where $n \geq 6$, preferably $n \geq 8$; and more preferably $n \geq 10$.

By "quantum dot" as that term is used herein, it is meant a semiconductor nanocrystal with size-dependent optical and electrical properties. In particular, the band gap energy of a quantum dot varies with the diameter of the crystal. In the
30 naming convention used herein to refer to coated nanocrystals, the compound found within parentheses represents the core compound (i.e. the quantum dot), while the compound which follows represents the overcoated layer. "Quantum yield" as that

term is used herein, means the ratio of photons emitted to that absorbed, e.g., the photoluminescence quantum yield.

In other embodiments of the invention, the coated nanocrystal is characterized in that the nanocrystal exhibits less than a 10% and preferably less than 5%, rms deviation in diameter of the core. The nanocrystal in an aqueous environment preferably exhibits photoluminescence having quantum yields of greater than 10%, and most preferably in the range of about 10 to 30%.

The invention permits the preparation of a water-soluble nanocrystal having a very narrow particle size distribution and exhibiting improvements in color purity and intensity of their photoluminescent emissions. Upon exposure to a primary light source, the quantum dot emits light of an energy characteristic of its composition and size.

These and other features and advantages of the invention are set forth in the description of the invention, which follows.

Brief Description of the Drawing

The invention is described with reference to the figures, which are presented for the purpose of illustration only, and in which:

Figure 1 is a schematic illustration of the water-soluble nanocrystal of the invention; and

Figure 2 is an illustration of the displacement reaction used in the formation of the water-soluble nanocrystal of the invention

Detailed Description of the Invention

Most prior art quantum dots are prepared in a coordinating solvent, resulting in the formation of a passivating organic layer on the dot surface comprised of the organic solvent. The passivated quantum dots thus are readily soluble in organic solvents, such as toluene, chloroform and hexane. The present invention provides a surface-modified particle that is soluble instead in aqueous media.

The nanocrystal is represented schematically in Figure 1. A semiconductor nanocrystal 10 is coated with an outer layer 14 that renders the crystal water-soluble. The outer layer 14 further is selected to maintain the luminescent properties of the

nanocrystal and to improve the robustness of the nanocrystal in aqueous solutions. An optional overcoating layer 12 may be used to coat the quantum dot before application of the outer layer 14. The outer layer includes a compound 15 of the formula, $\text{SH}(\text{CH}_2)_n\text{X}$, wherein X is carboxylate or sulfonate.

5 The nanocrystal includes a semiconductor nanocrystal that demonstrates quantum confinement effects in their luminescent properties. These nanocrystals are known as "quantum dots". When quantum dots are illuminated with a primary energy source, a secondary emission of energy occurs of a frequency that corresponds to the band gap of the semiconductor material used in the quantum dot. In quantum
10 confined particles, the band gap is a function of the size of the nanocrystal.

 Many semiconductors have been prepared as quantum sized particles and exhibit quantum confinement effects in their physical properties and can be used in the water-soluble nanocrystals of the invention. Exemplary materials suitable for use as quantum dots include ZnS, ZnSe, ZnTe, CdS, CdSe, CdTe, and ternary and
15 quaternary mixtures thereof.

 The semiconductor nanocrystals are characterized by their uniform nanometer size. By "nanometer" size, it is meant less than about 150 Angstroms (\AA), and preferably in the range of 12-150 \AA . The nanocrystal also is substantially monodisperse within the broad nanometer range given above. By monodisperse, as
20 that term is used herein, it is meant a colloidal system in which the suspended particles have substantially identical size and shape. For the purposes of the present invention, monodisperse particles mean that at least 60% of the particles fall within a specified particle size range. In preferred embodiments, monodisperse particles deviate less than 10% in rms diameter, and preferably less than 5%. Monodisperse
25 quantum dots have been described in detail in Murray *et al.* (*J. Am. Chem. Soc.*, 115:8706 (1993)), the thesis of Christopher Murray, Massachusetts Institute of Technology, September, 1995, *supra*, and Kuno *et al.*, *supra*, which are hereby incorporated in their entireties by reference.

 In preferred embodiments, the quantum dot has an overcoating layer. At the
30 surface of the quantum dot, surface defects can result in traps for electron or holes that degrade the electrical and optical properties of the quantum dot. An insulating layer at the surface of the quantum dot provides an atomically abrupt jump in the

chemical potential at the interface which eliminates energy states that can serve as traps for the electrons and holes. This results in higher efficiency in the luminescent process.

Suitable materials for the overcoating layer include semiconductors having a higher band gap energy than the quantum dot. In addition to having a band gap energy greater than the quantum dots, suitable materials for the overcoating layer should have good conduction and valence band offset with respect to the quantum dot. Thus, the conduction band is desirably higher and the valence band is desirably lower than those of the quantum dot. A material that has a band gap energy in the uv may be used. Exemplary materials include ZnS, GaN, and magnesium chalcogenides, e.g., MgS, MgSe and MgTe. The overcoating layer may include up to eight monolayers of the semiconductor material.

Particularly preferred quantum dots for emission in the visible include CdX, where X = S, Se and Te and ZnY, where Y = Se, Te. For those compounds, ZnS is a preferred material for use as the overcoating. For CdTe, ZnSe may be a preferred material for use as the overcoating due to the high degree of lattice match between the materials. A particularly preferred overcoated nanocrystal is described in Dabbousi *et al.* (*J. Phys. Chem. B* **101**(46):9463 (1997)), and Kuno *et al.*, *supra*, which are hereby incorporated in its entirety by reference.

According to the invention, the surface of the quantum dot is coated with the compound of the invention to stabilize the quantum dot in aqueous solution. The compound includes a sulfur group that attaches to the surface of the particle and a carboxylic acid group that is solvated in the aqueous media. The two groups are spanned by a hydrophobic region, $-(CH_2)_n-$. The hydrophobic region also provides a "pseudo-hydrophobic" environment for the nanocrystal and thereby shields it from its aqueous surroundings. To exhibit quantum size effects it is also necessary for the particles to remain electrically isolated from one another. The outer layer of the invention serves the additional useful purpose of maintaining the desired isolation between individual quantum dots.

The $-(CH_2)_n-$ group is selected to prevent photooxidation of the surface by charge transfer of a hole to the surface, whether from the core of the quantum dot or from the environment. Typical processes include electrolysis of water from the

environment with the resultant oxidation of sulfur or selenium (of the quantum dot) to SO_2 or SeO_2 , respectively. Transfer of a charge across the layer represents a non-energy emissive pathway for the excited state of the semiconductor and photoluminescence is thereby significantly reduced or quenched.

5 Prior art surface modifications of quantum dots included capping of CdS nanocrystals with 2-mercaptoethanol, 1-thioglycerol and 3-mercaptopropionic acid. See, Lawless, *et al.* and Rogach *et al.* These short chain organic molecules do not provide a luminescent, water-soluble quantum dot because the short carbon chain does not provide adequate insulation of the quantum dot to photooxidative processes.
10 Therefore, charge transfer occurs between the quantum dot and either the carboxylate or the aqueous environment. Luminescence is thereby quenched. Consequently, quantum yields are “unacceptably low”, i.e., less than 1%, in systems employing short chain organic molecules as a capping layer.

 According to the invention, the hydrophobic region is preferably a long chain
15 hydrocarbon moiety, $-(\text{CH}_2)_n-$, where n is greater than six and preferably greater than eight. Hydrocarbon moieties of $n = 11$ and 15 have been successfully used in the manufacture of the water-soluble nanocrystal of the invention. There is no upper limit to the hydrocarbon chain length; however, it is recognized that very long hydrocarbon chains might render the nanocrystal undesirably “greasy”. The
20 hydrophobic region also may include branching hydrocarbons.

 A method for the preparation of the water-soluble nanocrystal follows. The method is described for a (CdSe)ZnS quantum dot, but it is understood that the method may be applied in the preparation of quantum dots from the known semiconductor materials.

25 A population of nearly monodisperse nanocrystals first is prepared. The actual size of the nanocrystals will vary dependant upon the material used. For CdSe, particles range in size from about 12 Å to about 150 Å with a particle size distribution of about 5-10%. The monodisperse nanocrystals may be obtained by using a high temperature colloidal growth process, followed by size selective precipitation. In
30 those instances where narrow spectral emission bandwidths are desired, it is desirable to use size selective precipitation to obtain a population of quantum dots of narrow

particle size distribution. The interested reader is directed to Murray *et al.*, *supra*, and the thesis of Christopher Murray, for further information.

The quantum dot may then be coated with the appropriate semiconductor overcoating layer. The coated nanocrystal may be prepared by introducing the substantially monodisperse first semiconductor nanocrystal and a precursor capable of thermal conversion into a second semiconductor material into a coordinating solvent. The coordinating solvent is maintained at a temperature sufficient to convert the precursor into the second semiconductor material yet insufficient to substantially alter the monodispersity of the first semiconducting nanocrystal and the second semiconductor material has a band gap greater than the first semiconducting nanocrystal. An overcoating of the second semiconductor material is formed on the first semiconducting nanocrystal. The monodispersity of the nanocrystal is monitored during conversion of the precursor and overcoating of the first semiconductor nanocrystal. The particle size distribution may be further refined by size selective precipitation. Further details in the preparation of a coated quantum dot for use in the water-soluble nanocrystal of the invention may be found in U.S.S.N. 08/ 969,302, filed November 13, 1997 and entitled "Highly Luminescent Color-Selective Materials", and Dabbousi *et al.*, *supra*, which are incorporated in their entirety by reference.

The outer surface of the nanocrystal, as formed, includes an organic layer derived from the coordinating solvent used during the capping layer growth process. The nanocrystal surface may be modified to obtain the water-soluble nanocrystal of the invention by repeated exposure to an excess of a competing coordinating group. For example, a dispersion of the quantum dot may be treated with a coordinating organic compound, such as those described herein, to produce nanocrystals which dispersed readily in water, but which no longer disperse in aliphatics. Such a surface exchange process may be carried out using a variety of compounds which are capable of coordinating or bonding to the outer surface of the capped quantum dot, such as by way of example, phosphines, thiols, amines, phosphine oxides and amine oxides.

A typical reaction is shown in Figure 2. Quantum dots 60 are prepared in a coordinating organic solvent such as trioctylphosphine oxide (TOPO) which results in the formation of a passivating TOPO layer 62 on the semiconductor surface of the

quantum dot. This layer is displaced at least in part by the compound 54, a long chain mercaptocarboxylic acid, comprising the outer layer of the invention in order to obtain water-soluble nanocrystal 66. Displacement may occur by dispersion of quantum dots or overcoated quantum dots in medium containing high concentrations of the ligand used to form the outer coating. The medium may be a neat liquid comprising the ligand or it may be a highly concentration solution. High concentrations drive the displacement reaction forward to maximize surface coverage of the nanocrystal by the compound of the outer coating. Note that the displacement of the TOPO layer need not be complete in order to obtain a water-soluble nanocrystal.

It may be desirable to repeatedly expose the nanocrystal to the coordinating ligand solution. The outer coating may be comprised of a mixture of the original polar organic solvent used in the preparation of the nanocrystal and the water-solubilizing compound used in the outer coating of the invention. Substitution of the water-solubilizing compound need only be sufficient to render the compound water-soluble and need not be complete. In some embodiments, substitution is about 25-50% complete, preferably greater than 60% complete.

The example is illustrated in the following examples, which are presented for the purpose of illustration only and which are not limiting of the invention.

Example 1. Preparation of TOPO capped-(CdSe)ZnS

(a) Preparation of CdSe. Trioctylphosphine oxide (TOPO, 90% pure) and trioctylphosphine (TOP, 95% pure) were obtained from Strem and Fluka, respectively. Dimethyl cadmium (CdMe_2) and diethyl zinc (ZnEt_2) were purchased from Alfa and Fluka, respectively, and both materials were filtered separately through a 0.2:μm filter in an inert atmosphere box. Trioctylphosphine selenide was prepared by dissolving 0.1 mols of Se shot in 100ml of TOP thus producing a 1M solution of TOPSe. Hexamethyl(disilathiane) (TMS_2S) was used as purchased from Aldrich. HPLC grade n-hexane, methanol, pyridine and n-butanol were purchased from EM Sciences.

The typical preparation of TOP/TOPO capped CdSe nanocrystals follows. TOPO (30g) was placed in a flask and dried under vacuum (~1 Torr) at 180 °C for 1 hour. The flask was then filled with nitrogen and heated to 350 °C. In an inert

atmosphere drybox the following injection solution was prepared: CdMe_2 (200 microliters, 2.78 mmol), 1 M TOPSe solution (4.0 mL, 4.0 mmol), and TOP (16 mL). The injection solution was thoroughly mixed, loaded into a syringe, and removed from the drybox.

5 The heat was removed from the reaction flask and the reagent mixture was delivered into the vigorously stirring TOPO with a single continuous injection. This produces a deep yellow/orange solution with a sharp absorption feature at 470-500 nm and a sudden temperature decrease to $\sim 240^\circ\text{C}$. Heating was restored to the reaction flask and the temperature was gradually raised to $260\text{-}280^\circ\text{C}$.

10 Aliquots of the reaction solution were removed at regular intervals (5-10 min) and absorption spectra taken to monitor the growth of the crystallites. The best samples were prepared over a period of a few hours steady growth by modulating the growth temperature in response to changes in the size distribution, as estimated from the sharpness of the features in the absorption spectra. The temperature was lowered
15 5-10 $^\circ\text{C}$ in response to an increase in the size distribution. Alternatively, the reaction can also be stopped at this point. When growth appears to stop, the temperature is raised 5-10 $^\circ\text{C}$. When the desired absorption characteristics were observed, the reaction flask was allowed to cool to $\sim 60^\circ\text{C}$ and 20 mL of butanol were added to prevent solidification of the TOPO. Addition of a large excess of methanol causes the
20 particles to flocculate. The flocculate was separated from the supernatant liquid by centrifugation; the resulting powder can be dispersed in a variety of organic solvents (alkanes, ethers, chloroform, tetrahydrofuran, toluene, etc.) to produce an optically clear solution.

 (b) Preparation of (CdSe)ZnS. A flask containing 5g of TOPO was heated to
25 190EC under vacuum for several hours then cooled to 60EC after which 0.5 mL trioctylphosphine (TOP) was added. Roughly 0.1-0.4 :mols of CdSe dots dispersed in hexane were transferred into the reaction vessel via syringe and the solvent was pumped off.

 Diethyl zinc (ZnEt_2) and hexamethyldisilathiane ($(\text{TMS})_2\text{S}$) were used as the
30 Zn and S precursors, respectively. The amounts of Zn and S precursors needed to grow a ZnS shell of desired thickness for each CdSe sample were determined as follows: First, the average radius of the CdSe dots was estimated from TEM or SAXS

measurements. Next, the ratio of ZnS to CdSe necessary to form a shell of desired thickness was calculated based on the ratio of the shell volume to that of the core assuming a spherical core and shell and taking into account the bulk lattice parameters of CdSe and ZnS. For larger particles the ratio of Zn to Cd necessary to achieve the same thickness shell is less than for the smaller dots. The actual amount of ZnS that grows onto the CdSe cores was generally less than the amount added due to incomplete reaction of the precursors and to loss of some material on the walls of the flask during the addition.

Equimolar amounts of the precursors were dissolved in 2-4 mL TOP inside an inert atmosphere glove box. The precursor solution was loaded into a syringe and transferred to an addition funnel attached to the reaction flask. The reaction flask containing CdSe dots dispersed in TOPO and TOP was heated under an atmosphere of N₂. The temperature at which the precursors were added ranged from 140 °C for 23 Å diameter dots to 220 °C for 55 Å diameter dots. When the desired temperature was reached the Zn and S precursors were added dropwise to the vigorously stirring reaction mixture over a period of 5-10 minutes.

After the addition was complete the mixture was cooled to 90 °C and left stirring for several hours. Butanol (5mL) was added to the mixture to prevent the TOPO from solidifying upon cooling to room temperature. The overcoated particles were stored in their growth solution to ensure that the surface of the dots remained passivated with TOPO. They were later recovered in powder form by precipitating with methanol and redispersing into a variety of solvents including hexane, chloroform, toluene, THF and pyridine.

Example 2. Preparation of a water-soluble quantum dots using long chain mercaptocarboxylic acid.

TOPO capped-(CdSe)ZnS quantum dots were prepared as described in Example 1. The overcoated (CdSe)ZnS dots were precipitated from the growth solution using a mixture of butanol and methanol. To obtain the precipitated quantum dots, the solution was centrifuged for 5-10 min., the supernatant was decanted and the residue was washed with methanol (2X).

The residue was weighed. The weight of the TOPO cap was assumed to be 30% of the total weight; and a 30-fold molar excess of the new capping compound,

11-mercaptoundecanoic acid (MUA) was added. The residue and MUA (neat solution) were stirred at 60°C for 8-12 hours. A volume of tetrahydrofuran (THF) equal to the added MUA was added to the MUA/dot mixture, with the mixture was still hot. A clear solution resulted and the coated quantum dots were stored under
5 THF.

The coated quantum dots are rendered water-soluble by deprotonation of the carboxylic acid functional group of the MUA. The deprotonation was accomplished by adding a suspension of potassium *t*-butoxide in THF to the MUA-quantum dot/THF solution. A gel resulted, which was then centrifuged and the supernatant
10 liquid was poured off. The residue was washed twice with THF, centrifuged each time and the supernatant liquid poured off. The final residue was allowed to dry in air for 10 minutes. Deionized water (Millipore) was added to the residue until a clear solution formed.

The resultant coated quantum dots were tested for photoluminescent quantum
15 yield. A CdSe quantum dot with a four monolayer coating of ZnS coated as described had an absorption band a 480 nm and a photoluminescent band at 500 nm, with a quantum yield of 12%. A second CdSe quantum dot with a four monolayer coating of ZnS coated as described had an absorption band a 526 nm and a photoluminescent band at 542 nm, with a quantum yield of 18%.

20

What is claimed is:

- 1 1. A water soluble semiconductor nanocrystal capable of light emission,
2 comprising:
3 a quantum dot having a selected band gap energy;
4 a layer overcoating the quantum dot, the overcoating layer comprised of a
5 material having a band gap energy greater than that of the quantum dot;
6 an outer layer, the layer comprising a compound having the formula,
7 $\text{SH}(\text{CH}_2)_n\text{X}$, where X is carboxylate or sulfonate.
8
9 2. The water-soluble nanocrystal of claim 1, where $n \geq 8$.
10
11 3. The water-soluble nanocrystal of claim 1, where $n \geq 10$.
12
13 4. The water soluble nanocrystal of claim 1, wherein the quantum dot is a
14 member of a substantially monodisperse particle population.
15
16 5. The water soluble nanocrystal of claim 1, wherein when irradiated the
17 coated nanocrystal emits energy in a spectral range of no greater than about 60 nm at
18 full width half max (FWHM).
19
20 6. The water soluble nanocrystal of claim 1, wherein the nanocrystal exhibits
21 less than a 10% rms deviation in diameter of the quantum dot.
22
23 7. The water soluble nanocrystal of claim 1, wherein when irradiated the
24 coated nanocrystal emits energy in a spectral range of no greater than about 40 nm at
25 full width half max (FWHM).
26
27 8. The water soluble nanocrystal of claim 1, wherein t when irradiated the
28 coated nanocrystal emits energy in a spectral range of no greater than about 30 nm at
29 full width half max (FWHM).
30
31 9. The water soluble nanocrystal of claim 1, wherein the coated nanocrystal
32 exhibits photoluminescence having quantum yields of greater than 10% in water.

1 10. The water soluble nanocrystal of claim 1, wherein the coated nanocrystal
2 exhibits photoluminescence having quantum yields in the range of 10-30% in water.
3

4 11. The water soluble nanocrystal of claim 1, wherein the quantum dot
5 comprises YX, where Y is selected from the group consisting of Zn, Cd, and mixtures
6 thereof and X is selected from the group consisting of S, Se and Te and mixtures
7 thereof.
8

9 12. The water soluble nanocrystal of claim 1, wherein the overcoating layer is
10 comprises AB, where A is selected from the group consisting of Zn, Cd, and mixtures
11 thereof and B is selected from the group consisting of S, Se and Te, such that AB is
12 not the same as the quantum dot and AB has a higher band gap energy than the
13 quantum dot.
14

15 13. The water soluble nanocrystal of claim 13, wherein the overcoating layer
16 comprises up to eight monolayers of AB.
17

18 14. The water soluble nanocrystal of claim 1, wherein the spectral range of
19 emission is selected from the spectrum in the range of about 470 nm to about 650 nm.
20

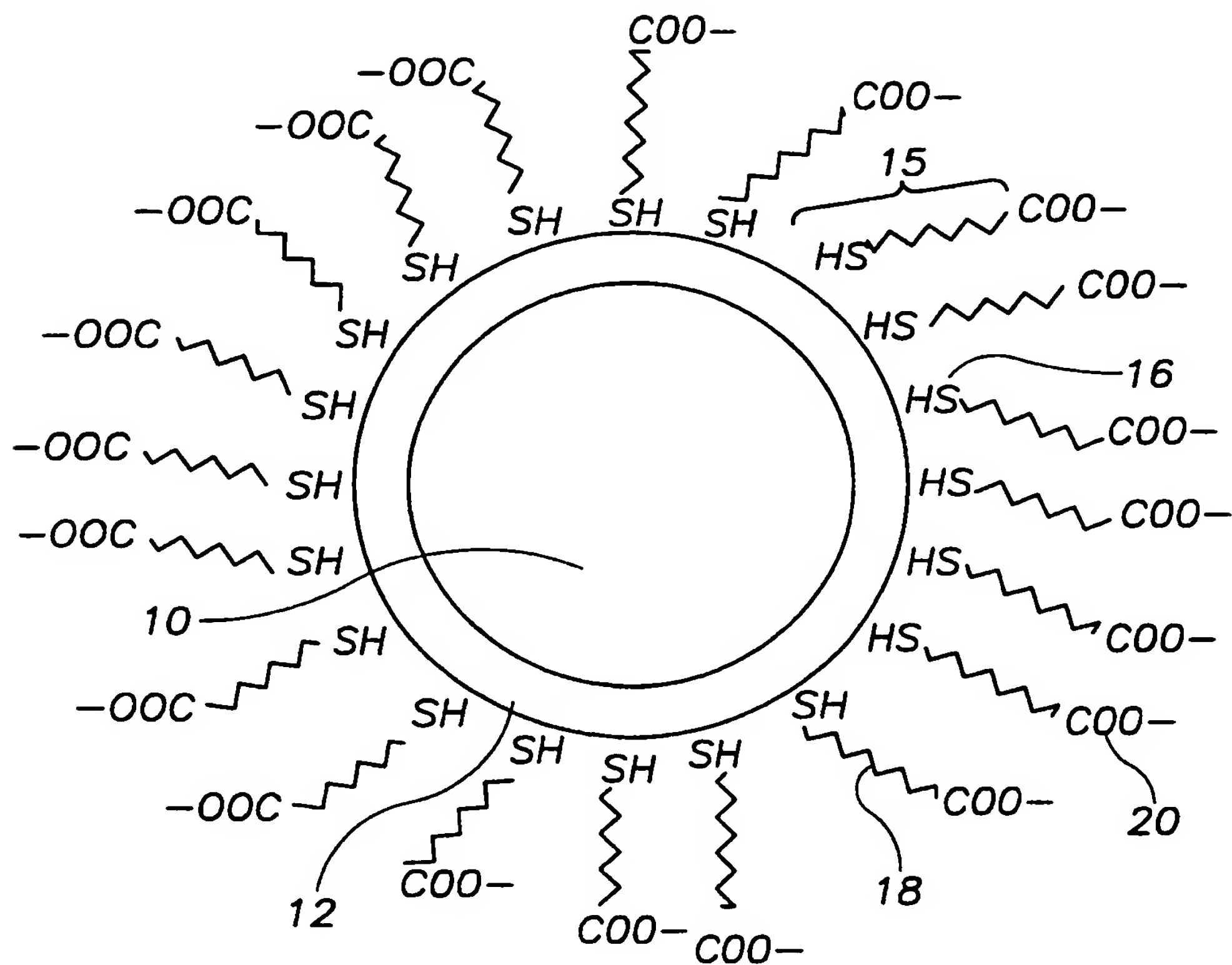
21 15. The water soluble nanocrystal of claim 1, wherein the particle size of the
22 core is selected from the range of about 12Å to about 150 Å.
23

24 16. A composition, comprising:

25 a water soluble nanocrystal including a quantum dot having a band gap energy
26 in the visible light range and at least one water-solubilizing moiety attached to the
27 outer surface of the quantum dot, the moiety having the formula, $\text{SH}(\text{CH}_2)_n\text{X}$, where
28 X is a hydrophilic moiety, the water soluble nanocrystal dispersed or dissolved in an
29 aqueous medium.

1/4

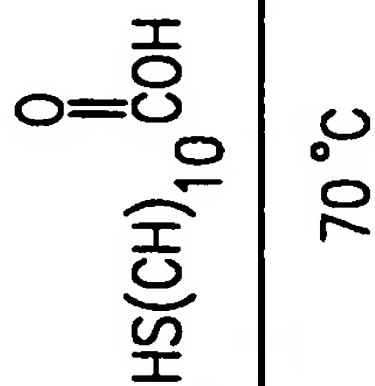
FIG. 1



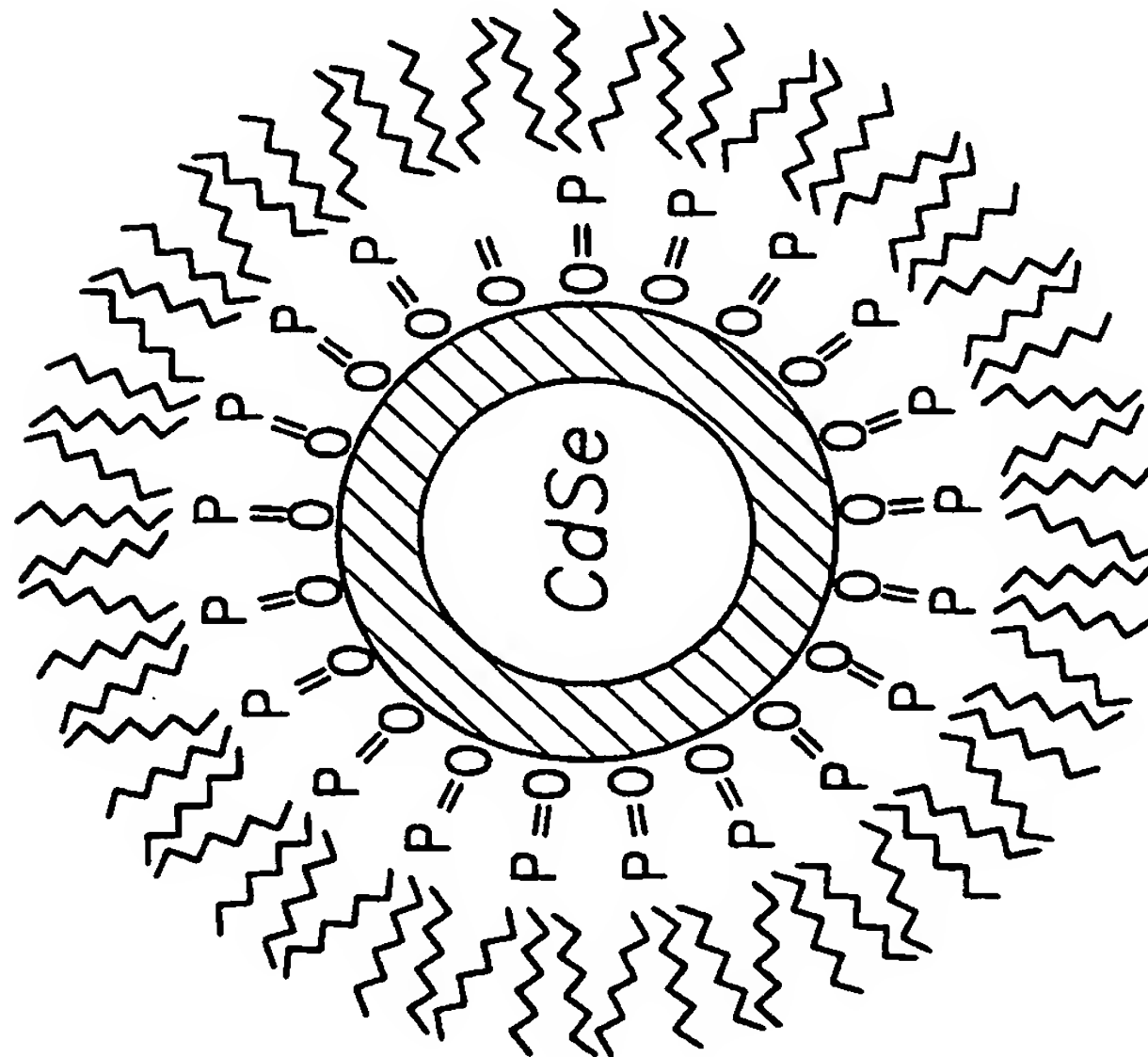
SUBSTITUTE SHEET (RULE 26)

2/4

TO
FIG. 2A



70°C



**HEXANE
SOLUBLE**

FIG. 2

SUBSTITUTE SHEET (RULE 26)

3/4

TO
FIG. 2A

BASE

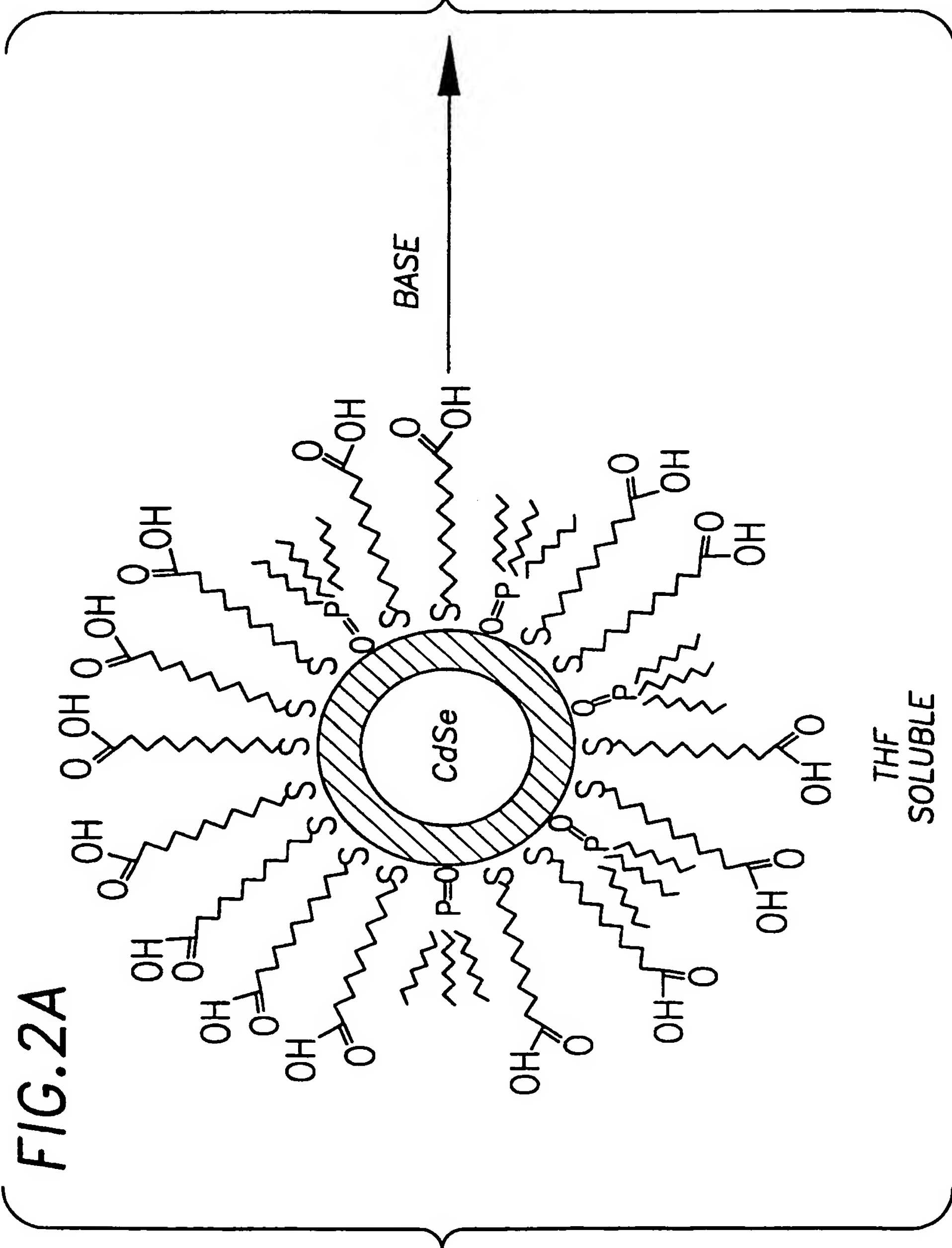
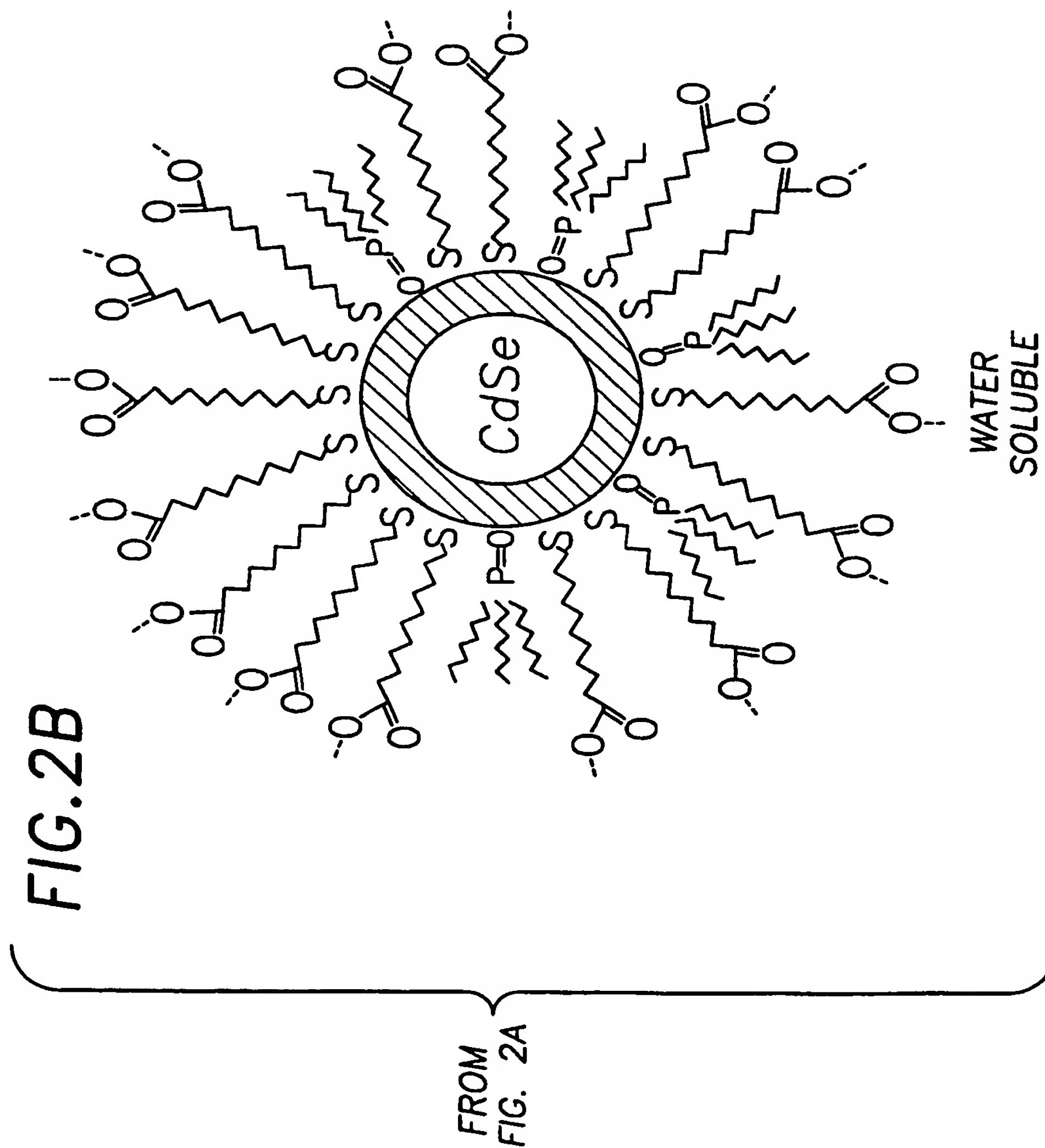


FIG. 2A

FROM
FIG. 2

4/4



INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/21493

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/58 H05B33/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N H01L H05B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>CHAN W C W ET AL: "Quantum dot bioconjugates for ultrasensitive nonisotopic detection"</p> <p>SCIENCE, 25 SEPT. 1998, AMERICAN ASSOC. ADV. SCI, USA, vol. 281, no. 5385, pages 2016-2018, XP002125871</p> <p>ISSN: 0036-8075</p> <p>the whole document</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	<p>1,4-8, 11,12, 14-16</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

17 January 2000

Date of mailing of the international search report

24/01/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

De Laere, A

INTERNATIONAL SEARCH REPORT

Inter: nal Application No

PCT/US 99/21493

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LAWLESS D ET AL: "Bifunctional capping of CdS nanoparticles and bridging to TiO ₂ " JOURNAL OF PHYSICAL CHEMISTRY, vol. 99, 1995, pages 10329-10335, XP000829587 AMERICAN CHEMICAL SOCIETY, US ISSN: 0022-3654 cited in the application abstract ---	1,4,11, 16
A	US 5 751 018 A (ALIVISATOS A PAUL ET AL) 12 May 1998 (1998-05-12) claims 17-41; figure 1 ---	1,2,4, 11,15,16
A	DABBOUSI B O: "(CDSE)ZNS CORE-SHELL QUANTUM DOTS: SYNTHESIS AND CHARACTERIZATIONS OF A SIZE SERIES OF HIGHLY LUMINESCENT NANOCRYSTALLITES" JOURNAL OF PHYSICAL CHEMISTRY. B, MATERIALS, SURFACES, INTERFACES AND BIOPHYSICAL,US,WASHINGTON, DC, vol. 101, no. 46, page 9463-9475 XP002095418 ISSN: 1089-5647 the whole document -----	1,4-8, 11-16

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 99/21493

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5751018 A	12-05-1998	EP 0613585 A	07-09-1994
		JP 7502479 T	16-03-1995
		WO 9310564 A	27-05-1993



P.B.5818 - Patentlaan 2
2280 HV Rijswijk (ZH)
☎ (070) 3 40 20 40
FAX (070) 3 40 30 16

Europäisches
Patentamt

European
Patent Office

Office européen
des brevets

Generaldirektion 1

Directorate General 1

Direction générale 1

Liesegang, Roland
FORRESTER & BOEHMERT
Pettenkoferstrasse 20-22
80336 München
ALLEMAGNE

FORRESTER & BOEHMERT

Eing.: 04. April 2006

Frist:



EPO Customer Services

Tel.: +31 (0)70 340 45 00

Date

04.04.06

Reference
FB12887

Application No./Patent No.
03019282.7 - 2203

Applicant/Proprietor
HITACHI SOFTWARE ENGINEERING CO., LTD.

COMMUNICATION

The European Patent Office herewith transmits as an enclosure the European search report (under R. 44 or R. 45 EPC) for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

- ☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

The following specifications given by the applicant have been approved by the Search Division :

- ☒ Abstract ☒ Title

- ☐ The abstract was modified by the Search Division and the definitive text is attached to this communication.

The following figure will be published together with the abstract : 1

Refund of search fee

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 03 01 9282

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X Y Y	WO 00/17656 A (MASSACHUSETTS INSTITUTE OF TECHNOLOGY) 30 March 2000 (2000-03-30) * page 10, line 20 - page 13, line 20 * ----- TORIMOTO T ET AL: "Characterization of ultrasmall CdS nanoparticles prepared by the size-selective photoetching technique" JOURNAL OF PHYSICAL CHEMISTRY. B, MATERIALS, SURFACES, INTERFACES AND BIOPHYSICAL, WASHINGTON, DC, US, vol. 105, no. 29, 26 July 2001 (2001-07-26), pages 6838-6845, XP002254498 ISSN: 1089-5647 * the whole document * -----	1 2,3 2,3	H01L51/00 C09C1/10
			TECHNICAL FIELDS SEARCHED (IPC)
			H01L C09C
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 9 March 2006	Examiner Königstein, C
<div>CATEGORY OF CITED DOCUMENTS</div> <div>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</div> <div>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</div>			

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 03 01 9282

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on

The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

09-03-2006

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0017656 A	30-03-2000	US 6426513 B1	30-07-2002